IOM: Congress must reform FDA to improve drug safety

Y ears of underfunding, inadequate resources, and a lack of clarity in the law combined with a growing complexity of drugs has left FDA in a weakened state, an Institute of Medicine (IOM) panel concluded in a long-anticipated report.

Infighting between FDA’s office that approves the marketing of medications and the office that oversees postmarketing safety has impeded the drug safety process, IOM’s Committee on the Assessment of the U.S. Drug Safety System said.

In addition, panelists said, a lack of transparency in the drug-approval process has damaged the agency’s credibility with the public.

“Anyone who has followed the drug safety saga of the last several years has surely noticed that information has emerged . . . about scientific disagreements poorly handled, a lack of collaboration among divisions, an appearance of disciplinary tension, a perception of inappropriate management expectations, and so on,” said Sheila Burke, chair of the committee that wrote the report.

The 15-member panel, which was commissioned by FDA to assess regulatory authorities, available resources, and the organizational structure of the Center for Drug Evaluation and Research (CDER) and make recommendations about improving the U.S. drug safety system, recommended sweeping reforms of the agency.

FDA has a great deal of power during the drug development and marketing approval processes, the committee noted.

But, panelists said, after a medication is approved for marketing, regulators must negotiate with pharmaceutical companies to voluntarily withdraw unsafe drugs or to add new warnings, precautions, or contraindications to labeling when safety issues about a medication are revealed.

In fact, the committee noted, the law allows FDA to institute recalls only for devices and baby formula.

Delaying approval until complete certainty is reached or withdrawing a drug once safety problems arise are often not realistic options, Burke told reporters at a September 22 media briefing.

Yet, she said, those options “reflect the largely all-or-nothing nature of FDA regulatory authorities.”

Panelist Alta Charo, law and bioethics professor at the University of Wisconsin at Madison, said that changes over the past 100 years in the statute that governs FDA’s authority has focused on enhancing postapproval powers.

But, she said, Congress has done little over the past century to strengthen FDA’s postapproval authorities.

“FDA’s authorities must be clarified and strengthened to empower the agency to take rapid and decisive actions when necessary and appropriate,” the committee told Congress.

Panelists found an imbalance in the regulatory attention and resources available before and after a drug’s approval, Burke said.

FDA staff and resources devoted to preapproval are substantially greater than those available for postapproval functions, she said.

Indeed, while CDER’s Office of New Drugs—the office that approves the marketing of medications—has about 700 employees, the Office of Surveillance and Epidemiology, which oversees postmarketing safety reviews, has only about 100.

FDA has become increasingly dependent on funding from the Prescription Drug User Fee Act (PDUFA)—a system whereby drug companies pay fees to FDA to support its process for reviewing applications for new drugs and biologicals, the committee asserted.

PDUFA’s emphasis on the speed of drug approvals has created tension inside the agency, panelists argued, adding that appropriations from Congress for FDA have remained roughly flat since PDUFA was enacted in 1992.

“User fees have led to an overall increase in resources for new drug review, but activities not funded by user fees have received a smaller portion of FDA’s total budget,” the committee said.

FDA’s limited resources could impede the agency’s ability to detect risks of new drugs in a timely fashion, analyze emerging drug safety data, and effectively communicate that information to the public, panelists said.

The committee called on Congress to substantially increase funding for FDA and recommended that the agency’s drug safety activities be supported by appropriations from general revenues rather than PDUFA user fees.

“Congressional appropriations from general tax revenues are a mechanism by which the public can directly, fairly, and effectively invest in the FDA’s postmarket drug safety activities,” panelists said.

The committee suggested that a small tax on prescriptions could generate significant funding.

“A tax of ten cents on every prescription,” panelists said, “would generate more than $100 million for the FDA budget.”

The committee acknowledged that such a tax would likely have an effect on the costs of and access to medications.

Promotions

Stacey Henning, Pharm.D., was promoted to the rank of Commander in the U.S. Public Health Service. Henning is a clinical pharmacy specialist at the National Institutes of Health Clinical Center in Bethesda, Maryland.

Thomas J. McGinnis was promoted to the rank of Assistant Surgeon General and Rear Admiral in the U.S. Public Health Service. McGinnis is chief of Pharmaceutical Operations Directorate, Tricare Management Activity, Department of Defense, Falls Church, Virginia.
Also among the IOM committee’s recommendations was a suggestion that FDA’s commissioner be appointed to a six-year term.

The committee noted that over the past 30 years, FDA has had eight commissioners and seven acting commissioners. The eight commissioners served an average of 2.5 years, with a range of two months to 6.3 years.

“A large, complex, science-based regulatory agency cannot perform optimally in the absence of stable, capable leadership, and clear, consistent direction,” panelists stated.

Former National Cancer Institute Director Andrew von Eschenbach has been serving in an acting capacity as FDA commissioner since fall 2005 after the abrupt departure of Lester Crawford, who resigned two months after being confirmed to the job, reportedly because of financial conflicts of interest.

“Without stable leadership strongly and visibly committed to drug safety, all other efforts to improve the effectiveness of the agency or position it effectively for the future will be seriously, if not fatally, compromised,” panelists wrote.

The expectation of a six-year term, Burke said, “helps to avoid some of the tension that exists in positions that naturally turnover automatically in the case of the change of administrations.”

“It also sends a message that the priority ought to be placed on the selection of an individual who is qualified based on their scientific credentials,” she added.

The committee also recommended that Congress amend the Federal Food, Drug, and Cosmetic Act to require that product labeling for new drugs, new combinations of active substances, and new systems of delivery of existing drugs carry a special symbol, such as the black triangle used in the United Kingdom or an equivalent symbol, to denote that there is limited knowledge about the risks associated with those products.

The symbol, panelists said, should remain on drug labeling and related materials for two years, unless FDA chooses to shorten or extend the period on a case-by-case basis.

In addition, the committee said, FDA should restrict direct-to-consumer advertising during the period of time the special symbol is in effect.

The IOM panel’s recommendations, said Henri R. Manasse Jr., executive vice president and chief executive officer of the American Society of Health-System Pharmacists (ASHP), align with ASHP’s policies.

“The IOM committee’s recommendations rightly place a greater emphasis on the life cycle of a drug product, rather than just the approval phase,” he said. “This broader approach will help protect patients and make significant strides toward a safe and effective medication-use system.”

—Donna Young

DOI 10.2146/news060016

Health disparities affect cancer rates in Hispanics

Hispanics living in the United States had lower rates of most cancers from 1999 through 2003 than non-Hispanic whites, the National Cancer Institute (NCI) reported in September.

However, the agency said in its annual report to the nation, during that same time period, U.S. Hispanic residents had higher rates of myeloma and cancers of the stomach, liver, and cervix than did non-Hispanic whites.

In addition, Hispanic men and women in the United States were more likely to be diagnosed with metastatic cancer than non-Hispanic white residents.

According to NCI, the number of new cases of different types of cancers varied among four Hispanic ethnic groups living in the United States: Mexican, Puerto Rican, Central American, and South American.

Therefore, the agency said, since not all populations share the same origins, cultural traditions, and immigration status, risks may be different for Hispanics of different ethnicities.

Factors that may contribute to the differences in the cancer rates of Hispanics living in the United States include elevated exposures to environmental risk factors in living areas and workplaces for that group, language barriers, reduced use of screening services, limited access to health care, lack of insurance, less information available about genetic predispositions, lower education, health literacy, and income levels.

Many types of cancers with higher incidence rates in Hispanics are associated with infections, such as human papilloma virus (HPV) in cervical cancer, Helicobacter pylori in stomach cancer, and hepatitis B and C in liver cancer, NCI reported.

“Public health interventions that may reduce infection-related cancers among U.S. Hispanic populations include immunization against hepatitis B and the most common oncogenic strains of HPV, screening and counseling for hepatitis B and C, and screening for cervical cancer,” the agency stated.

Cancer in Hispanic children. The incidence of specific cancers differed substantially among Hispanic and non-Hispanic white children and adolescents, officials said.